



Impact of Post-Antibiotic Effect Induced by Clindamycin and Chlorhexidine on the Virulence Factors of Oral Streptococci and Staphylococci

Thesis submitted by

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Contents

No.		Pages
	INTRODUCTION	1
1.	LITERATURE REVIEW	4
1.1.	History of Post-antibiotic effect	4
1.2.	Mechanism of Post-antibiotic Effect:	5
1.3.	Factors affecting the duration of PAE <i>in-vitro</i> :	9
1.3.1	Type of microorganism and antimicrobial agent.	9
1.3.2	Concentration of the antimicrobial agent.	10
1.3.3	Length of the antimicrobial exposure.	12
1.3.4	Post-exposure to sub-MICs.	13
1.3.5	Re-exposures {repeated antimicrobial agent}.	15
1.3.6	Type of culture medium.	16
1.3.7	Effect of pH.	18
1.3.8	Effect of temperature.	19
1.3.9	Effect of growth phase of the organism	20
1.3.10	Effect of oxygen.	20
1.3.11	Effect of mechanical shaking.	21
1.3.12	Effect of inoculum size.	21
1.3.13	The specific microorganism-antimicrobial combination.	22
1.4.	Antimicrobial Susceptibility of Dental Infection.	23

1.4.1.	Activity of clindamycin against oral bacteria.	23
1.4.2.	Tissue concentrations of clindamycin.	25
1.5.	Clindamycin in the Treatment of Dental Infections	26
1.5.1.	Acute dental infection	26
1.6.	Topical antiseptics	26
1.6.1.	Chlorhexidine antimicrobial activity	27
1.7.	Impact of PAE on Virulence Factors	29
1.7.1.	Cell Morphology and Ultrastructure	31
1.7.2.	Cell Surface Hydrophobicity	34
1.7.3.	Bacterial Adherence	35
1.7.4.	Enzyme Production	39
1.7.5.	Hemolysin Production	41
1.7.6.	Toxin Production	42
1.7.7.	Bactericidal Activity	43
1.7.8.	PAE and clinical trials	45
2.	MATERIALS AND METHODS	48
2.1.	Chemicals	48
2.2.	Media	48
2.3.	Buffers	50
2.4.	Antimicrobial agents	52
2.5.	Bacterial cultures	52

2.6.	Determination of minimum inhibitory concentration	56
2.7.	Determination of Post-antibiotic effect	57
2.8.	Scanning electron microscopy	60
2.9.	Cell Surface Hydrophobicity	61
2.10.	Elastase production	62
2.11.	Haemolysin production	63
3.	RESULTS	64
3.1.	Isolation of Bacteria	64
3.2.	Purification and maintenance	64
3.3.	Identification of the bacterial isolates	64
3.4.	Determination of the MIC	68
3.5.	Determination of the PAE	71
3.6.	Relation between MIC (sub and supra-MIC) and PAE	90
3.7.	Impact of PAE on virulence factors	91
4.	DISCUSSION	116
5.	SUMMARY	131
6.	REFERENCES	135
7.	ARABIC SUMMARY	

List of tables

Table No.		Page No.
Table (1)	Determination of MICs of staphylococcal isolates against clindamycin and chlorhexidine	69
Table (2)	Determination of MICs of streptococcal isolates against clindamycin and chlorhexidine	70
Table (3)	PAE induced by clindamycin against staphylococcal isolates	81
Table (4)	PAE induced by chlorhexidine against staphylococcal isolates	82
Table (5)	PAE induced by clindamycin against streptococcal isolates	87
Table (6)	PAE induced by chlorhexidine against streptococcal isolates	88
Table (7)	Effect of clindamycin at a concentration of 2XMIC and 1/2XMIC on (CSH) of <i>Staphylococcus aureus</i> (isolate 2 and 4) during PAE period	96
Table (8)	Effect of chlorhexidine at a concentration of 2XMIC on (CSH) of <i>Staphylococcus aureus</i> (isolate 2 and 4) during PAE period	97
Table (9)	Effect of combination of clindamycin/chlorhexidine at a concentration of 2XMIC on (CSH) of <i>Staphylococcus aureus</i> (isolate 2 and 4) during PAE period	98
Table (10)	Effect of clindamycin at a concentration of 2XMIC and 1/2XMIC on (CSH) of <i>Streptococcus mutans</i> (isolate 2 and 4) during PAE period	99

Table No.		Page No.
Table (11)	Effect of chlorhexidine at a concentration of 2XMIC on (CSH) of <i>Streptococcus mutans</i> (isolate 2 and 4) during PAE period	100
Table (12)	Effect of combination of clindamycin/chlorhexidine at a concentration of 2XMIC on (CSH) of <i>Streptococcus mutans</i> (isolate 2 and 4) during PAE period	101
Table (13)	Elastase production by staphylococcal isolates during PAE induced by clindamycin at different concentrations	103
Table (14)	Elastase production by streptococcal isolates during PAE induced by clindamycin at different concentrations	104
Table (15)	Elastase production by streptococcal isolates during PAE induced by chlorhexidine at different concentrations	105
Table (16)	Elastase production by staphylococcal isolates during PAE induced by combination of both clindamycin and chlorhexidine at 2XMIC	106
Table (17)	Elastase production by streptococcal isolates during PAE induced by combination of both clindamycin and chlorhexidine at 2XMIC	107
Table (18)	Hemolysin production by staphylococcal isolates during PAE induced by clindamycin at different concentration	110
Table (19)	Hemolysin production by streptococcal isolates during PAE induced by clindamycin at different concentration	111
Table (20)	Hemolysin production by staphylococcal isolates during PAE induced by chlorhexidine at different concentration	112
Table (21)	Hemolysin production by streptococcal isolates during PAE induced by chlorhexidine at different concentration	113

Table No.		Page No.
Table (22)	Hemolysin production by staphylococcal isolates during PAE induced by combination of both clindamycin and chlorhexidine at 2XMIC	114
Table (23)	Hemolysin production by streptococcal isolates during PAE induced by combination of both clindamycin and chlorhexidine at 2XMIC	115

List of figures

Figure No.		Page No.
Figure (1)	Growth of <i>Streptococcus mutans</i> on Mitis Salivarius Agar (blue gum drop shape).	54
Figure (2)	Catalase test of <i>Staphylococcus aureus</i> (A) and <i>Streptococcus mutans</i> (B).	66
Figure (3)	Hemolysis on blood agar; α -hemolysis of <i>Staphylococcus aureus</i> (A) and β -hemolysis of <i>Streptococcus mutans</i> (B).	67
Figure (4)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 2 to 2XMIC clindamycin.	74
Figure (5)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 2 to 4XMIC clindamycin.	75
Figure (6)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 2 to 1/2XMIC clindamycin.	75
Figure (7)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 2 to 1/2XMIC clindamycin.	76
Figure (8)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 4 to 4XMIC clindamycin.	76
Figure (9)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 4 to 8XMIC clindamycin.	77
Figure (10)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 4 to 1/2XMIC clindamycin.	77
Figure (11)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 4 to 1/4XMIC clindamycin.	78
Figure (12)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 2 to 2XMIC chlorhexidine.	78

Figure No.		Page No.
Figure (13)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 2 to 1/2XMIC chlorhexidine.	79
Figure (14)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 4 to 2XMIC chlorhexidine.	79
Figure (15)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 4 to 1/2XMIC chlorhexidine.	80
Figure (16)	PAEs induced by 1 h exposure of <i>Streptococcus mutans</i> 2 to 1/2XMIC clindamycin	83
Figure (17)	PAEs induced by 1 h exposure of <i>Streptococcus mutans</i> 2 to 1/4XMIC clindamycin.	83
Figure (18)	PAEs induced by 1 hour exposure of <i>Streptococcus mutans</i> 4 to 2XMIC clindamycin.	84
Figure (19)	PAEs induced by 1 hour exposure of <i>Streptococcus mutans</i> 4 to 4XMIC clindamycin.	84
Figure (20)	PAEs induced by 1 hour exposure of <i>Streptococcus mutans</i> 4 to 8XMIC clindamycin.	85
Figure (21)	PAEs induced by 1 hour exposure of <i>Streptococcus mutans</i> 4 to 1/2XMIC clindamycin.	85
Figure (22)	PAEs induced by 1 hour exposure of <i>Streptococcus mutans</i> 4 to 1/4XMIC chlorhexidine.	86
Figure (23)	PAEs induced by 1 hour exposure of <i>Staphylococcus aureus</i> 2 to 2XMIC clindamycin/chlorhexidine combination	89
Figure (24)	A and B: - Transmission electron microscopy of morphological changes induced by clindamycin or chlorhexidine against <i>Staphylococcus aureus</i> , compared to untreated cells, during PAE period	92

Figure No.		Page No.
Figure (25)	C: - Transmission electron microscopy of morphological changes induced by clindamycin against <i>Streptococcus mutans</i> , compared to untreated cells, during PAE period	93
Figure (26)	D: - Transmission electron microscopy of morphological changes induced by clindamycin and chlorhexidine against <i>Staphylococcus aureus</i> , compared to untreated cells, during PAE period	94

INTRODUCTION

The post-antibiotic effect (PAE) appears to be a phenomenon that represents a suppression of bacterial growth after exposure to antibiotic for a specific period. The period of growth suppression is related to the target site of antibiotic as well as the type of microorganisms. Thus protein synthesis inhibitors are usually prolonged PAE period especially against gram-positive bacteria. While cell wall synthesis inhibitors are usually induced short or even no PAE period against gram-negative bacteria (Rayner and Munckhof, 2005 & Hanberger *et al.*, 1991).

Several factors affecting the presence and/or the duration of PAE these factors are:

- (i) Type of microorganism
- (ii) Type of antimicrobial agent and its concentration
- (iii) Exposure time and
- (iv) Antimicrobial combination.

Other factors affecting duration of PAE such as: (i) Temperature; (ii) Oxygen level; (iii) Growth medium; and (iv) pH of the medium. The duration of PAE is varied according to the type of antibiotic as well as the type of the organism, Thus protein synthesis inhibitors are usually produced longer period against gram-positive bacteria.

Exposure of oral *Staphylococcus aureus* and *Streptococcus mutans* to a clindamycin at a concentration of one µg/ml For 1 hour induced long PAE period.

This period seems that it is a concentration dependent with most of antibiotics.

Actually clindamycin showed a considerable and concentration dependent PAEs against gram-positive cocci, especially streptococci and staphylococci (Drinkovic *et al.*, 2001).

The importance of PAE as a pharmacodynamic parameter is primary related to its potential influence on antimicrobial dosing regimen in clinical practice. Agent inducing a long PAE may be administered with longer dosing intervals without loss of efficacy. This integrates the microbiological and pharmacokinetics properties of antibiotics to predict the best dosage schedules that will provide maximal efficacy and minimal toxicity.

Clindamycine is commonly used systematically in the treatment of oral infectious diseases and other diseases, resulted from infection with anaerobic and gram-positive infections. This antibiotic is commonly used systematically in combination with chlorhexidine, in the form of mouthwash (Rask *et al.*, 1988).

Therefore, the study was conducted to determine the PAE induced by clindamycine and/or chlorhexidine against oral streptococci and staphylococci. The study was focused on the physiological changes that are occurred during and after PAE period.

Such changes represent the main virulence factors of staphylococci and streptococci, namely: cell morphology; cell adherence; enzyme production and toxin productions.

The following methodologies will be carried out to achieve the above objectives; including:

- i. Isolation of streptococcus and staphylococcus species from clinical specimens

- ii. Determination of susceptibilities of the recovered isolates against clindamycin and/or chlorhexidine, by determination of MICs (minimum inhibitory concentration) for the recovered isolates, according to the method recommended by NCCLS (2004)
- iii. Determination of PAE period by determination of the changes in the viable counts, and/or spectrophotometric technique for growth turbidity, before and after removal of the antibiotic
- iv. Determination of physiological changes in: (I) cell morphology, (II) cell adherence), (III) enzyme production and (IV) hemolysin production before and after PAE period.

1. Literature Review

1.1. History of Post-antibiotic Effect:

The post-antibiotic effect (PAE) is the term used to describe suppression of bacterial growth that persists after brief exposure of organisms to antimicrobial agent (Spangler *et al.*, 1998). In 1944, Bigger noted delayed development in turbidity after adding penicillinase to culture of staphylococci previously exposed to penicillin G. after few years Parker and Luse, (1948) and Parker and Marsh, (1946) noticed that staphylococci shortly exposed to penicillin and transferred to a drug free medium did not resume normal growth for up to three hours. Other investigator like Eagle and co-workers confirmed and extended these observations with penicillin to staphylococci and streptococci both *in-vitro* and *in-vivo* (Eagle *et al.*, 1950 & Eagle and Musselman, 1949).

It was observed that most antimycobacterial drugs induced an extended bacterial lag of regrowth (Mitchinson and Dickinson, 1971). However, it is not until the mid-1970s that these initial observations on the PAE were applied to gram-negative bacteria and antimicrobials developed after penicillin (McDonald *et al.*, 1977; Rolinson *et al.*, 1977). Thus, during the past two decades, PAE has been proved in almost every bacteria-drug combination tested.